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10/803,280	03/18/2004	Julia Golova	21416-05302	5570

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EXAMINER

LUNDGREN, JEFFREY S

ART UNIT PAPER NUMBER

1639

MAIL DATE DELIVERY MODE

07/16/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/803,280

Applicant(s)

GOLOVA ET AL.

Examiner

Jeff Lundgren

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 April 2007.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) 7-9 and 13-25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 10-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 7/14/04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

Election and Status of Claims

Applicant's election without traverse of: 1) Group I, claims 1-12; and 2) the species of compound 4 as identified in the specification at paragraph 00064, in the reply filed on April 27, 2007, is acknowledged.

Claims 1-25 are pending in the instant application, and claims 13-25 are withdrawn as being directed to a non-elected invention. Claims 7-9 are withdrawn as being directed to a non-elected species; claims 1-6 and 10-12 are the subject of the Office Action below.

Objection to the Abstract Under 37 C.F.R. § 1.72

The abstract of the disclosure is objected to because it does not allow the public generally to determine quickly from a cursory inspection the nature and gist of the invention. Applicants should amend the abstract so that it corresponds to at least one independent claim. For example, Applicants should describe the compound in claim 1 and each of the substituents. *See* 37 C.F.R. § 1.72. Should Applicants amend the claims in their next reply, the amended abstract should take into account any further limitations added to the broadest independent claim.

Objection of the Specification Under 37 C.F.R. §§ 1.821 - 1.825

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). *See*, for example, the nucleotide sequence on page 12 (paragraph 00066). However, this application fails to comply with the requirements of 37 CFR §§ 1.821 through 1.825 because this sequence contains greater than or equal to 10 nucleotide molecules and does not have a SEQ ID NO. A thorough review and correction throughout the application is required.

Applicants are given the same response time regarding this failure to comply as that set forth to respond to this Office Action. Failure to respond to this requirement may result in abandonment of the instant application or a notice of a failure to fully respond to this Office Action.

Information Disclosure Statement

The information disclosure statement filed February 3, 2003, fails to fully comply with 37 CFR § 1.98(b)(5), which requires that Applicants identify all non-patent literature listed in an information disclosure statement by publisher, author, title, relevant pages of the publication, date, and place of publication. Specifically, Applicants have not identified the dates that non-patent references by author Combs, and the cited pages from the Product Catalog of Glen Research, Inc., were made publicly available. See MPEP § 609.04(a).

Accordingly, these references have been lined through and have not been considered. See MPEP § 609.01.

Claim Rejections - 35 USC § 102

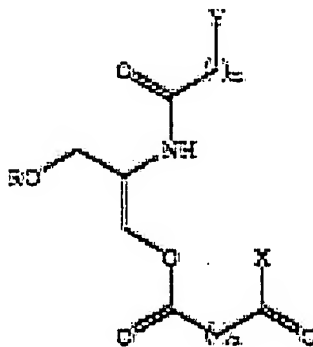
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 are rejected under 35 U.S.C. § 102(b) as being anticipated by Vu *et al.*, *Bioconjugate Chem.* 6:599-607 (1995).

Claim 1 is directed to a linker compound of formula:



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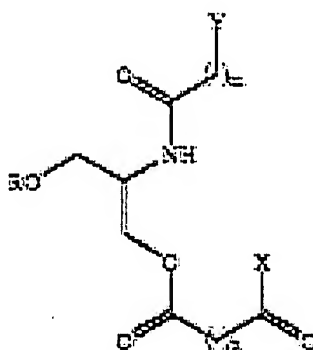
wherein R is selected from the group consisting of hydrogen and an oxygen protecting group, m and n are integers independently selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, and 8; X is an optionally substituted first heteroatom; and Y is an optionally substituted second heteroatom. Claim 2 differs wherein Y is an optionally substituted nitrogen or an optionally protected nitrogen.

Vu teaches the compounds of claims 1 and 2 (see compound 32¹ in Figure 1 on page 604); claims 1 and 2 read on Vu's compound when Y is an optionally substituted second heteroatom (Vu's substituted nitrogen); when R is an oxygen protecting group (Vu's DMT); when X is an optionally substituted heteroatom (Vu's amino-linked controlled pore glass – this disclosure also meets the limitations of claim 3-6).

Accordingly, claims 1-6 are anticipated by Vu.

Claims 1-6 are rejected under 35 U.S.C. § 102(b) as being anticipated by Mullah *et al.*, U.S. Patent No. 5,736,626, issued on April 7, 1998.

Claim 1 is directed to a linker compound of formula:

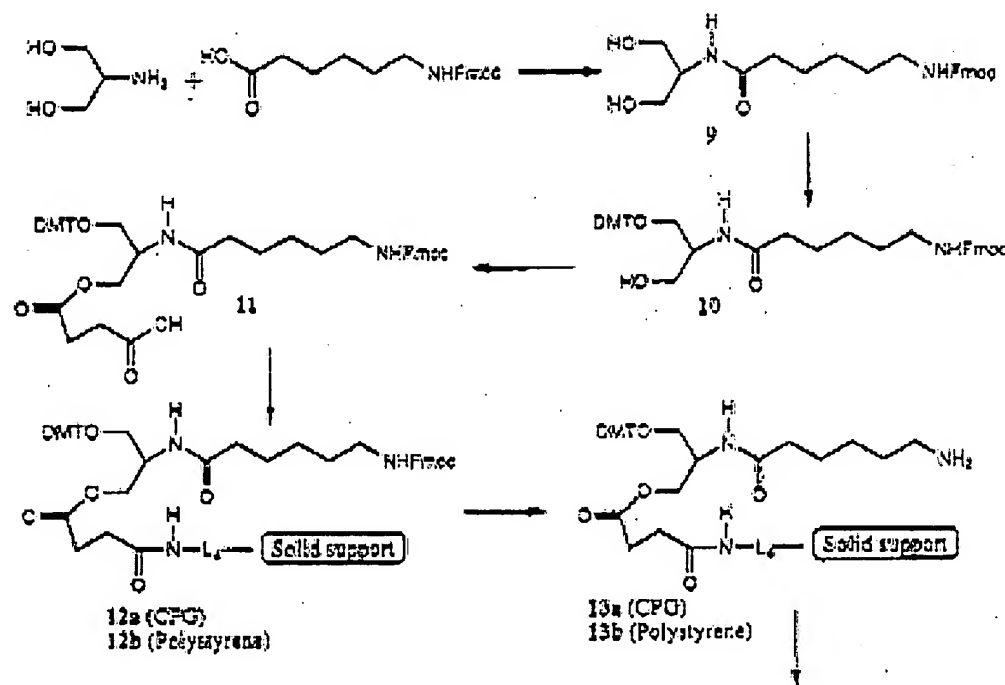


wherein R is selected from the group consisting of hydrogen and an oxygen protecting group, m and n are integers independently selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, and 8; X is an optionally substituted first heteroatom; and Y is an optionally substituted second

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heteroatom. Claim 2 differs wherein Y is an optionally substituted nitrogen or an optionally protected nitrogen.

Mullah teaches compounds exemplified by the class of diglycolate synthesis supports particularly useful as support reagents for the direct synthesis of 3'-labeled polynucleotides. In particular, Mullah teaches the compounds as shown below taken from Figure 1:



Similar to the comparison of Vu, the compounds taught by Mullah meet the limitations of claims 1 and 2 (each of compounds 11, 12 and 13, as shown in Figure 1).

Mullah also teaches attachment of the linker compound to the solid support of controlled-pore glass (col. 6, lines 1-4), and therefore meets the limitations of claims 3-6.

Accordingly, claims 1-6 are anticipated by Mullah.

¹ Compound having the registry number: 170941-85-2; CN: *N*-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]glycyl-*N*-[2-[bis(4-methoxyphenyl)phenylmethoxy]-1-[(3-carboxy-1-oxopropoxy)methyl]ethyl]-Glycinamide

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6 and 10-12 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Mullah et al., U.S. Patent No. 5,736,626, issued on April 7, 1998, in view of Vu *et al.*, *Bioconjugate Chem.* 6:599-607 (1995).

The limitations of claims 1-6 and corresponding teachings of Vu and Mullah are detailed above, and are incorporated into the instant rejection.

Mullah also teaches that part of the chemistry used to attach the linker to the solid support involves a succinate, such as for attachment *via* the L4 part of the compound (col. 7, lines 35-40), and therefore meets the limitation for group X' in claim 10. Mullah also teaches compounds that have the value for $m = 5$, and $n = 2$, which is required by claims 10 and 11.

And although Mullah teaches nitrogen protecting groups such as Fmoc and others, Mullah does not explicitly teach the chemical group TFA as required by claim 10 and claim 11 (*i.e.*, $-\text{C}(\text{O})\text{CF}_3$):

"If a reactive amino group is desired subsequent to polynucleotide cleavage [*sic*], R_1 and R_2 should not substantially interfere with the nitrogen reactivity. In this case, one of R_1 and R_2 is preferably lower alkyl, hydrogen, or a nitrogen protecting group, e.g., ***FMOC, tBOC, or other like nitrogen protecting groups***. Most preferably, one of R_1 and R_2 is hydrogen."

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Mullah, col. 8, lines 21-27 (emphasis added).

Vu's compounds share a substantial chemical core with those of Mullah², and are useful for the same purpose (e.g., synthesizing oligonucleotides on a solid support, and having a protected amino group that can be deprotected at a later point, then labeled). In addition to teaching Fmoc as an amino protecting groups, Vu also teaches TFA protecting groups, such as those shown in compound 19 (see Figure 1, page 604).

One of ordinary skill in the art would have had a reasonable expectation of success in arriving at the invention as claimed because each of Mullah and Vu teach chemical linking compounds for building oligonucleotides on solid supports with amino protecting groups that can be selectively removed and labeled. One of ordinary skill in the art would have been motivated to utilize other protecting groups with the core compound of Mullah, such as the TFA group as taught by Vu, because of the advantages rapid cleavage of TFA in basic environments (Vu, pages 606, cols. 1 and 2). Such an approach allows for subsequent cleavage and labeling with components of the linker molecule that are otherwise unstable in the presence of an acid, yet stable in the presence of a base (e.g., the chemistry involving the solid support or oligonucleotide). Therefore, the invention as a whole was *prima facie* obvious at the time it was invented.

Common Ownership of Claimed Invention Presumed

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. §§ 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

² Compare Vu's compounds 19 in Figure 1 on page 604, with Mullah's compound 12 in Figure 1. The main difference is the Fmoc protecting group instead of TFA, and a C5 attachment of the protecting group.

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Conclusions

No claim is allowable.

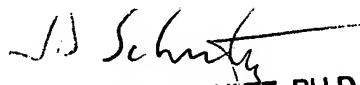
If Applicants should amend the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (*e.g.*, if the amendment is not supported *in ipsius verbis*, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeff Lundgren whose telephone number is 571-272-5541. The Examiner can normally be reached from 7:00 AM to 5:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, James Schultz, can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSL


J. DOUGLAS SCHULTZ, PH.D.
SUPERVISORY PATENT EXAMINER